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Jay Akhave
Signature _____ *Date* 9.14.04

13 September, 2004

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P O Box 1450
Alexandria
VA 22313-1450

Sub: Certified Foreign Priority Document on U.S. Application 10/634,978

Dear Sir:

This is a submission of certified priority documents for the following U.S. Patent application.

U S Patent Application No.	10/634,978
Filing Date	8/4/2003
Title	A novel crystalline form of Cefdinir
First named Inventor	Ramesh Dandala
Art Unit	1614
Attorney Docket No.	2003-015
Filing Status	Filed awaiting First office Action

Sincerely,

Jay Akhave
845 Pomello Dr
Claremont CA 91711
909 625 3492
US Patent Agent No 50,016

Encl: Certified Copy of Indian Application No. 440/MAS/2003

THE PATENTS ACT, 1970

It is hereby certified that annexed hereto is a true copy of Application, Complete Specification, Abstract & Drawings of the extract of Patent Application No.440/MAS/2003, dated 02/06/2003 by Aurobindo Pharma Limited having its registered office at Plot No.2, Maitrivihar Complex, Ameerpet, Hyderabad – 500 038, Andhra Pradesh, India.

.....

.....**In witness thereof**

I have hereunto set my hand

Dated this the 21st day of June 2004

M.S. Venkataraman

(M.S. VENKATARAMAN)
ASSISTANT CONTROLLER OF PATENTS & DESIGNS

ATEN FFICE BRANCH
OVER ENT OF INDIA
ana Co lex, 6th Floor, Annex.II
.443, a Salai, Teynampet,Chennai – 600 018

FORM 1

THE PATENTS ACT, 1970
(39 of 1970)
APPLICATION FOR GRANT OF A PATENT OFFICE
[See section 5(2), 7, 54 and 135]

1. We,

AUROBINDO PHARMA LIMITED
PLOT NO. 2, MAITRIVIHAR COMPLEX (Regd. Office)
AMEERPET
ANDHRA PRADESH
HYDERABAD – 500 038
INDIA
(An Indian Organization)

2. Hereby declare: -

(a) That we are in possession of an invention titled: -

(b) "PROCESS FOR THE PREPARATION OF NOVEL CRYSTALLINE FORM OF CEFDINIR."

(c) That the Complete Specification relating to this invention is filed with this application.

(d) That there is no lawful ground of objection to grant of a Patent to us.

3. Further declare that the inventor(s) for the said invention is: -

(a) RAMESH DANDALA

(b) MEENAKSHISUNDERAM SIVAKUMARAN

C/o. AUROBINDO PHARMA LIMITED
PLOT NO. 2, MAITRIVIHAR COMPLEX (Regd. Office)
AMEERPET
ANDHRA PRADESH
HYDERABAD – 500 038.
INDIA

(a) to (b) : All residents and citizens of India

4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows:-

(a) NIL

(b) NONE

5. We state that the said invention is an improvement in or modification of the particulars of
which are as follows and of which we are the Applicant/Patentee:

(a) NIL

(b) NONE

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application be deemed to have been filed on
.....
..... under section 16 of the Act:

NONE

7. That we are the assignee or legal representative of the true and first Inventors.

8. That our addresses for service in India is as follows:

AUROBINDO PHARMA LIMITED
Plot No. 2, Maitrivihar Complex,
Ameerpet
Andhra Pradesh
Hyderabad - 500 038
India
Phone No.: 91-40-23741083
Fax No. : 91-40-23741080, 23740591

9. Following declaration was given by the inventor(s) or applicant(s) in the convention country:-

NONE

We the true and first inventors for the invention, declare that the applicant(s) herein are our assignee

(a) RAMESH DANDALA

(b) MEENAKSHISUNDERAM SIVAKUMARAN

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Following are the attachment with the application: -

(a) Complete Specification (3 copies).

(b) Drawings (Nil)

(c) Priority document(s)

(d) Fee Rs. 5000/- in Bank Draft bearing No..... dated 1-06-03 on State Bank of Hyderabad.

We request that a Patent may be granted to us for the said invention.

Dated this 30th day of May 2003.

AUROBINDO PHARMA LTD. INDIA HYDERABAD

(Dr. M. SIVAKUMARAN)
DIRECTOR

TO
THE CONTROLLER OF PATENTS,
THE PATENT OFFICE,
CHENNAI

Form-2

THE PATENT ACT, 1970

COMPLETE

SPECIFICATION

(SECTION 10)

TITLE

"PROCESS FOR THE PREPARATION OF NOVEL CRYSTALLINE FORM OF CEFDINIR"

APPLICANT

AUROBINDO PHARMA LIMITED
HAVING REGISTERED OFFICE AT
PLOT NO. 2, MAITRI VIHAR COMPLEX,
AMEERPET, HYDERABAD – 500 038,
ANDHRA PRADESH, INDIA,
AN INDIAN ORGANIZATION

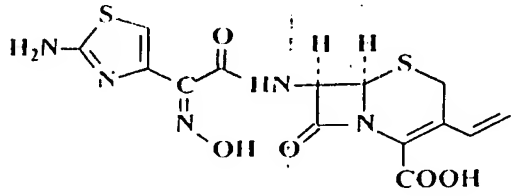
The following specification particularly describes and ascertains the nature of this invention and the manner in which the same is to be performed.

FIELD OF THE INVENTION

The present invention relates to the process for the preparation of novel crystalline form of Cefdinir, 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid.

BACKGROUND OF THE INVENTION

Cefdinir of Formula I is a very useful antimicrobial agent and is chemically known as 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid.



Formula I

Cefdinir is an oral antibiotic and was first disclosed in US patent 4,559,334. The product obtained according to above invention was crystalline like amorphous product, not a crystalline product.

US patent 4,935,507 discloses the methods of producing crystalline cefdinir that offered better filtration rate, high purity and stable cefdinir suitable for pharmaceutical preparation. This was prepared by treating amorphous cefdinir with sodium bicarbonate solution and the resulting aqueous solution was subjected to column chromatography and then adjusting the pH between 1-2 at 35-40°C followed by cooling to obtain cefdinir crystal A. Alternatively, amorphous cefdinir was dissolved in methanol and to this solution added water at 35°C, stirred and allowed to stand at room temperature to obtain cefdinir crystal A.

Though, US patent 4,935,507 claims crystalline form A, advantages may yet be realized by others, heretofore undiscovered forms of cefdinir. The present invention includes a novel crystalline form of cefdinir. Polymorphism is the property of some molecules and molecular complexes to assume more than one crystalline or amorphous form in solid state. A molecule like cefdinir of Formula I may give to a variety of solids having distinct physical properties like solubility, melting point, powdered X-ray diffractogram (XRD). The differences in the physical properties of polymorphs result from the orientation and intermolecular interactions of adjacent molecules (complexes) in the bulk solid. Accordingly, polymorphs are distinct solids sharing the same molecular formula, which may be thought of as analogous to unit cell metallurgy, yet having distinct advantageous and or disadvantageous physical properties compared to other forms in the polymorph family. The present invention provides a new crystalline form of cefdinir having moisture content in the range of 5.5-7.0%, but typically 6-7%, amounting closely to sesquihydrate and herein called as cefdinir crystal B. Further, the major advantages realized in the present invention are avoiding the use of chromatographic technique and highly pure cefdinir crystal B is obtained. It is an objective of the present invention to provide a stable, nontoxic, non-solvate crystalline modification of cefdinir, which is substantially free of impurities.

BRIEF DESCRIPTION OF ACCOMPANYING DRAWINGS

Fig. 1 is a characteristic X-ray powder diffractogram of cefdinir crystal B

Vertical axis: Intensity (CPS)
Horizontal axis: Two theta (degrees)

The significant d values (2θ) obtained are 5.8±0.2, 11.7±0.2, 16.1±0.2, 18.6±0.2, 20.9±0.2, 22.2±0.2, 24.4±0.2, 25.6±0.2 etc.

Fig. 2 is a X-ray powder diffractogram of cefdinir crystal A

Vertical axis: Intensity (CPS)
Horizontal axis: Two theta (degrees).

The significant d value (2θ) obtained are 11.7±0.2, 14.7±0.2, 17.8±0.2, 21.5±0.2, 21.9±0.2, 23.4±0.2, 24.5±0.2, 25.4±0.2 etc.

Fig. 3 is the infrared absorption spectrum of cefdinir crystal B.

Fig. 4 is the infrared absorption spectrum of cefdinir crystal A.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to the process for the preparation of a novel crystalline form of cefdinir, hereinafter called as cefdinir crystal B. More particularly, the novel form may contain water up to 5.5-7.0% by weight but typically close to 6.3% w/w which corresponds to the stoichiometric value of ~1.5 mole of water per mole of cefdinir. The novel crystal B of cefdinir of the present invention may be characterized by powdered X-ray diffraction and infrared absorption spectrum. Thus powdered X-ray diffraction of novel cefdinir crystal B and crystal A were determined on Seifert XRD 3003TT system using a copper target X-ray tube, a nickel filter and the sample was placed in a pyrex glass holder. The scan rate was 1.8 degrees, two theta per minute with the step size of 0.03 degrees two theta over the range from 5 to 50 degrees.

The novel cefdinir crystal B has powdered X-ray diffraction pattern essentially as shown in Table 1 and the powdered X-ray diffraction pattern reported for crystal A is given in Table 2. The powdered X-ray diffraction patterns are expressed in terms of two theta and relative intensities.

TABLE-1 : LIST OF 2θ AND RELATIVE INTENSITY FOR CEFDINIR CRYSTAL B.

2θ	*RELATIVE INTENSITY (%)*
5.8	25
7.7	31
8.0	31
11.7	100
15.6	42
16.1	61
18.6	44
19.4	25
21.0	34
21.2	44
22.3	61
24.4	44
25.6	38

TABLE-2: LIST OF 2θ AND RELATIVE INSENTIES FOR CEFDINIR CRYSTAL A

2θ	*RELATIVE INTENSITY (%)*
6.9	9
8.8	8
11.7	21
12.5	19
14.7	89
16.5	20
17.8	59
18.8	22
21.5	100
21.9	73
23.4	42
24.5	87
25.4	20

The infrared absorption spectra of cefdinir crystal B and crystal A were determined on Perkin Elmer-spectrum ONE infrared spectrophotometer.

The infrared absorption spectrum of cefdinir crystal B (Fig 3) shows characteristics peaks at 1017, 1049, 1121, 1134, 1191, 1428, 1545, 1613, 1667, 1780, 3295 and 3595 Cm^{-1}.

Whereas the infrared spectrum of cefdinir crystal A (Fig 4) shows characteristics peaks at 1013, 1175, 1460, 1519, 1556, 1594, 1622, 1682 and 1766 Cm^{-1}.

It is evident from the above data that the novel crystalline form of present invention is different from the cefdinir crystal A reported in US patent 4,935,507. The powdered X-ray diffraction pattern of crystal B shows maximum peak at 11.7±0.2 degree two theta whereas crystal A shows maximum peak at 21.5±0.2 degree two theta. We have found that this novel cefdinir crystal B has excellent storage stability characteristics and suitable for pharmaceutical formulation.

The stress stability studies of cefdinir crystal B were carried out. The samples were kept under the conditions of 60°C±2°C and the purity and assay of samples were determined before and after the stress test by high performance liquid chromatography and given in Table 3.

TABLE-3: STRESS STABILITY DATA OF CEFDINIR CRYSTAL B

Sample	Purity (by HPLC)		Assay (by HPLC) on anhydrous basis	
	Initial	After stress test	Initial	After stress test
1	99.66%	99.45%	99.9%	100.75%
2	99.71%	99.38%	99.4%	99.52%

As shown in the Table-3 even after keeping the samples at 60°C±2°C for fifteen days the compounds have not degraded. Therefore, it is evident that cefdinir crystal B is quite stable.

The process comprises the step of condensation of 7-amino-3-vinyl-3-cephem-4-carboxylate 4-methoxybenzyl ester hydrochloride with 2-benzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-trityloxyiminothioacetate in the presence of trialkylamine in any suitable solvent such as *N,N*-dimethylacetamide, *N,N*-dimethylformamide, methylene dichloride and like and mixture thereof. Specifically the condensation is carried out at a temperature range of 40-50°C. After completion of reaction, the reaction mass is cooled and product is extracted into suitable organic solvent and washed with dilute base and water. The suitable solvent can be selected from methylene dichloride, chloroform, toluene, ethylene dichloride etc., most preferably methylene dichloride. Further, organic layer is treated with trifluoroacetic acid at a temperature of about 10-15°C for 4-5 h to remove carboxyl protecting groups. Thereafter, the organic layer was cooled to 0°C and water was added. The layers were separated, and on cooling the aqueous layer, trifluoroacetic acid salt of cefdinir precipitated out, which is isolated by filtration.

Further, the wet cefdinir trifluoroacetic acid salt is suspended in water and neutralized with aqueous ammonia at a temperature of 0-30°C most preferably at 20-25°C to obtain highly purified cefdinir crystal B.

A further aspect of the present invention is a process to produce cefdinir crystal B from cefdinir crystal A.

The process comprises of suspending cefdinir crystal A in water at 35-40°C and treating with trifluoroacetic acid to prepare cefdinir.trifluoroacetic acid salt. The trifluoroacetic acid salt of cefdinir is isolated in high purity. Typically purity is analyzed by HPLC and is greater than 99.5% and generally closer to 99.6%. The trifluoroacetic acid salt of cefdinir is then neutralized by adjusting the pH to 3.0-3.2 with aqueous ammonia in water at 0-30°C preferably at 20-25°C to obtain highly pure cefdinir crystal B as off white solid. Typically, the purities are greater than 99% by HPLC in commercial lots. The trifluoroacetic acid salt of cefdinir is preferably used as wet material without drying.

The cefdinir crystal A can be prepared by methods known in the art (US 4,935,507) and then can easily be converted to cefdinir crystal B.

The present invention hence provides a novel crystalline form, crystal B of cefdinir and a method of its preparation, which is amenable to large-scale production, and suitable for formulation.

The novel crystalline form, crystal B of cefdinir of the present invention is readily filterable and easily dried. Moreover, the cefdinir crystal B prepared is of high purity typically greater than 99.5% as seen by HPLC. The novel crystalline form shows excellent storage stability and hence suitable for formulation. The novel crystal B of cefdinir may contain 5.5-7.0% of water and has a decomposition range of 188-192°C.

Having thus described the various aspects of the present invention, the following examples are provided to illustrate specific embodiments of the present invention. They are not intended to be limiting in anyway.

Example 1

STEP-I

PREPARATION OF 7β-[(Z)-2-AMINO-4-THIAZOLYL)-2-HYDROXYIMINOACETAMIDO]-3-VINYL-3-CEPHEM-4-CARBOXYLIC ACID.TRIFLUOROACETIC ACID SALT (CEFDINIR.TRIFLUOROACETIC ACID SALT)

50 g of 7-Amino-3-vinyl-3-cephem-4-carboxylate-4-methoxybenzyl ester hydrochloride (0.130 mol) and 71.5 g of 2-benzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-trityloxyimino-thioacetate (0.124 mol) were suspended in 250 ml of *N,N*-dimethylacetamide and 12.5 g of triethylamine (0.124 mol) was added thereto. Then the mixture was stirred for 3 hours at 40-50°C. After cooling to 10°C, methylene dichloride (750 ml) was added followed by demineralised water (1000 ml) and stirred for 10 minutes at the same temperature. Layers were separated and the organic layer was washed with dilute sodium hydroxide solution and water respectively. The methylene dichloride layer was cooled to 10°C. Trifluoroacetic acid (300 ml) was added over a period of 30 minutes at 10-15°C and stirred for 4 hours at the same temperature. Thereafter, cooled the reaction solution to 0°C. Demineralised water (875 ml) was added and separated the layers. Aqueous extract was cooled to 0°C and stirred for 60 minutes. The precipitate thus obtained was filtered and washed with ice-cooled water (125 ml) to obtain trifluoroacetic acid salt of cefdinir as an off white crystalline solid having purity 99.5% by HPLC.

^{1}H-NMR in *DMSO-d_6* : *δ(ppm): 3.58 and 3.83 (Abq, 2H, J=17.84), 5.20 (d, 1H, J=4.94 Hz), 5.32 (d, 1H, J=11.25 Hz), 5.60 (d, 1H, J=17.56 Hz), 5.79 (dd, 1H, J=4.94 Hz and 8.23 Hz), 6.76 (s, 1H), 6.92 (dd, 1H, J=11.25 Hz and 17.56 Hz), 9.60 (d, 1H, J=7.96 Hz)*

STEP-II

PREPARATION OF 7β-[(Z)-2-(2-AMINO-4-THIAZOLYL)-2-HYDROXYIMIN ACETAMIDO]-3-VINYL-3-CEPHEM-4-CARBOXYLIC ACID (CEFDINIR CRYSTAL B)

The wet product 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid.trifluoroacetic acid salt obtained in Example-1 was suspended in water (875 ml) and cooled to 10°C. pH was adjusted to 3.0-3.2 with aqueous ammonia solution at 20-25°C and filtered, washed with water (250 ml) and thus dried to obtain 24 g of cefdinir crystal B as a off white solid. (HPLC Purity: 99.6%).

Water content (% w/w, by KF): 7.0%; Melting point: 190°C (decompose).

^{1}H-NMR in *DMSO-d_6* : *δ(ppm); 3.55 and 3.84 (Abq, 2H, J=17.56 Hz), 5.19 (d, 1H, J=4.94 Hz), 5.31 (d, 1H, J=11.25 Hz), 5.59 (d, 1H, J=17.56 Hz), 5.79 (dd, 1H, J=4.94 Hz and 8.23 Hz), 6.66 (s, 1H), 6.90 (dd, 1H, J=11.25 Hz and 17.56 Hz), 7.13 (bs, 2H), 9.48 (d, 1H, J=8.23 Hz).*

Example 2

STEP-I

PREPARATION OF 7β-[(Z)-2-(2-AMINO-4-THIAZOLYL)-2-TRITYLOXYIMINOACETAMIDO]-3-VINYL-3-CEPHEM-4-CARBOXYLIC ACID

25 g of 7-amino-3-vinyl-3-cephem-4-carboxylic acid and 65 g of 2-benzothiazolyl-(*Z*)-2-(2-amino-4-thiazolyl)-2-trityloxyiminothioacetate and 50 g of monotrimethylsilylacetamide were suspended in 165 ml of *N,N*-dimethylacetamide at 25°C. The mixture was stirred for 2 hours at 25-30°C, a solution of 25 g of *p*-toluenesulphonic acid monohydrate in methanol (25 ml) was added and the resulting solution was stirred for 15 min. Thereafter, 350 ml of diethylether was added and stirred for 30 min. The precipitate thus obtained was filtered, washed subsequently with 100 ml of diethylether and 100 ml of ethyl acetate. Dried the product to obtain 100 g of *p*-TSA.2DMAc salt of the title compound as a pale yellow solid.

The above *p*-TSA.2DMAc salt was added to a mixture of methylene dichloride (400 ml) and water (200 ml) at 25-30°C. To this mixture, sodium hydroxide solution (3.6 g sodium hydroxide dissolved in 25 ml water) was added in 15 min at 25-30°C and stirred the solution for 15 min at 25-30°C. The methylene dichloride layer was separated and concentrated to 200 ml. The concentrated mass was poured into hexanes (500 ml) in 30 min at 25-30°C. The precipitate thus obtained was filtered, washed with hexanes (100 ml) and dried to obtain 62 g of the title compound as a off-white crystalline solid (yield: 88%).

HPLC Purity: 97%

STEP-II

PREPARATION OF 7β-[(Z)-2-(2-AMINO-4-THIAZOLYL)-2-HYDROXYIMINOACETAMIDO]-3-VINYL-3-CEPHEM-4-CARBOXYLIC ACID (CEFDINIR CRYSTAL A)

50 g of 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-trityloxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid obtained in Step-I was added into a mixture of formic acid (75 ml) and water (75 ml) at 18-20°C in small lots to get a hazy solution and the solution was stirred for 5 hours at 18-20°C. The precipitate thus obtained was filtered off, washed with 50% aqueous formic acid (25 ml). The filtrate was cooled to 10-15°C and the pH was adjusted to 4.5 with 15 ml of ammonia solution at 10-15°C. The solution thus obtained was treated with carbon at 10-15°C. Carbon was filtered, washed with water (50 ml). The filtrate was warmed to 40°C and pH of the solution was adjusted to 2.8-3.0 with concentrated sulphuric acid. The crystals thus obtained was filtered, washed with water (250 ml) and dried to get 15 g of 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (Cefdinir crystal A, yield: 48%). HPLC Purity: 98%.

Water content: <1.0%; Melting Point: 175°C (decompose)

IR (Cm^{-1}, KBr): 1766, 1683, 1622, 1596, 1555, 1520

STEP-III

PREPARATION OF 7β-[(Z)-2-(2-AMINO-4-THIAZOLYL)-2-HYDROXYIMINO ACETAMIDO]-3-VINYL-3-CEPHEM-4-CARBOXYLIC ACID (CEFDINIR CRYSTAL B)

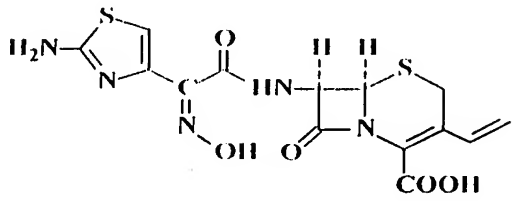
10 g of Cefdinir crystal A was suspended in 300 ml of demineralised water at 30-35°C. 30 ml of trifluoroacetic acid was added in 15 minutes at 30-35°C to get a clear solution. After about 15-20 minutes, precipitation was started and stirred for 60 minutes at 40°C. Precipitate thus obtained, was filtered, washed with chilled water (20 ml) to obtain trifluoroacetic acid salt of cefdinir. This salt without further drying was suspended in demineralised water (200 ml) at 20-25°C and the pH was adjusted to 3.0-3.2 with aqueous ammonia solution at 20-25°C. Stirred the resulting slurry for 30 minutes, filtered, washed with water (50 ml) and dried to get cefdinir crystal B as a off white solid. (HPLC Purity: 99.6%)

Water content (% w/w, by KF): 6.67%; Melting point: 190°C (decompose)

^{1}H-NMR in *DMSO-d_6* *δ(ppm); 3.56 and 3.84 (Abq, 2H, J=17.56 Hz), 5.19 (d, 1H, J=4.94 Hz), 5.31 (d, 1H, J=11.25 Hz), 5.59 (d, 1H, J=17.56 Hz), 5.79 (dd, 1H, J=4.94 Hz and 8.23 Hz), 6.67 (s, 1H), 6.91 (dd, 1H, J=11.25 Hz and 17.56 Hz), 7.15 (bs, 2H), 9.50 (d, 1H, J=8.23 Hz).*

WE CLAIM:

1. A process for the preparation of novel crystalline form of cefdinir, crystal B of 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid of Formula I,

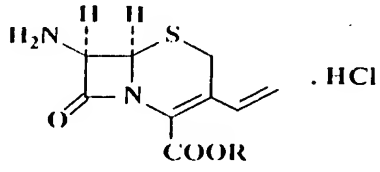


Formula I

which comprises the step of neutralizing cefdinir trifluoroacetic acid salt with a base such as ammonia, at a temperature of 0-30°C and preferably at 20-25°C and isolating the Cefdinir Crystal B, by conventional methods.

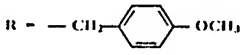
2. A process according to claim 1, wherein the cefdinir trifluoroacetic acid salt is prepared by the process which comprises the steps of;

- reacting 7-amino-3-vinyl-3-cephem-4-carboxylate-4-methoxybenzylester hydrochloride of Formula II

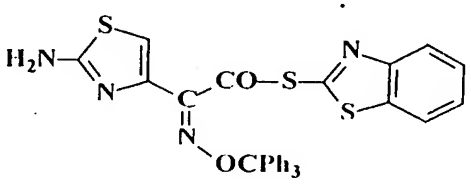


. HCl

Formula II

wherein R = 

with 2-benzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-trityloxyiminothioacetate of Formula III



Formula III

Ph - Phenyl

in the presence of trialkylamine in any suitable solvent at a temperature range of 40-50°C,

- extracting the protected cefdinir into a organic solvent like methylene dichloride, chloroform, toluene and mixture thereof and treating with trifluoroacetic acid to remove protecting group and isolating cefdinir as trifluoroacetic acid salt.

3. The process according to claim 2, wherein the reaction is carried out in *N,N*-dimethylformamide, *N,N*-dimethylacetamide, methylene dichloride and preferably *N,N*-dimethylacetamide is used.

4. The process according to claim 1, wherein the Cefdinir Crystal B obtained is having water in the range of 5.5-7%.

5. A process according to claim 1, wherein the Cefdinir trifluoroacetic acid salt is prepared by the process, which comprises:

- treating cefdinir crystal A in water with trifluoroacetic acid at a temperature of 35- 40°C,
- stirring for further 1-2 hours till crystallization of Cefdinir trifluoroacetic acid salt completes and
- isolating the cefdinir trifluoroacetic acid salt by filtration in high purity.

Dated this the 30th day of May 2003

AUROBINDO PHARMA LIMITED,

Dr. M. SIVAKUMARAN,
DIRECTOR.

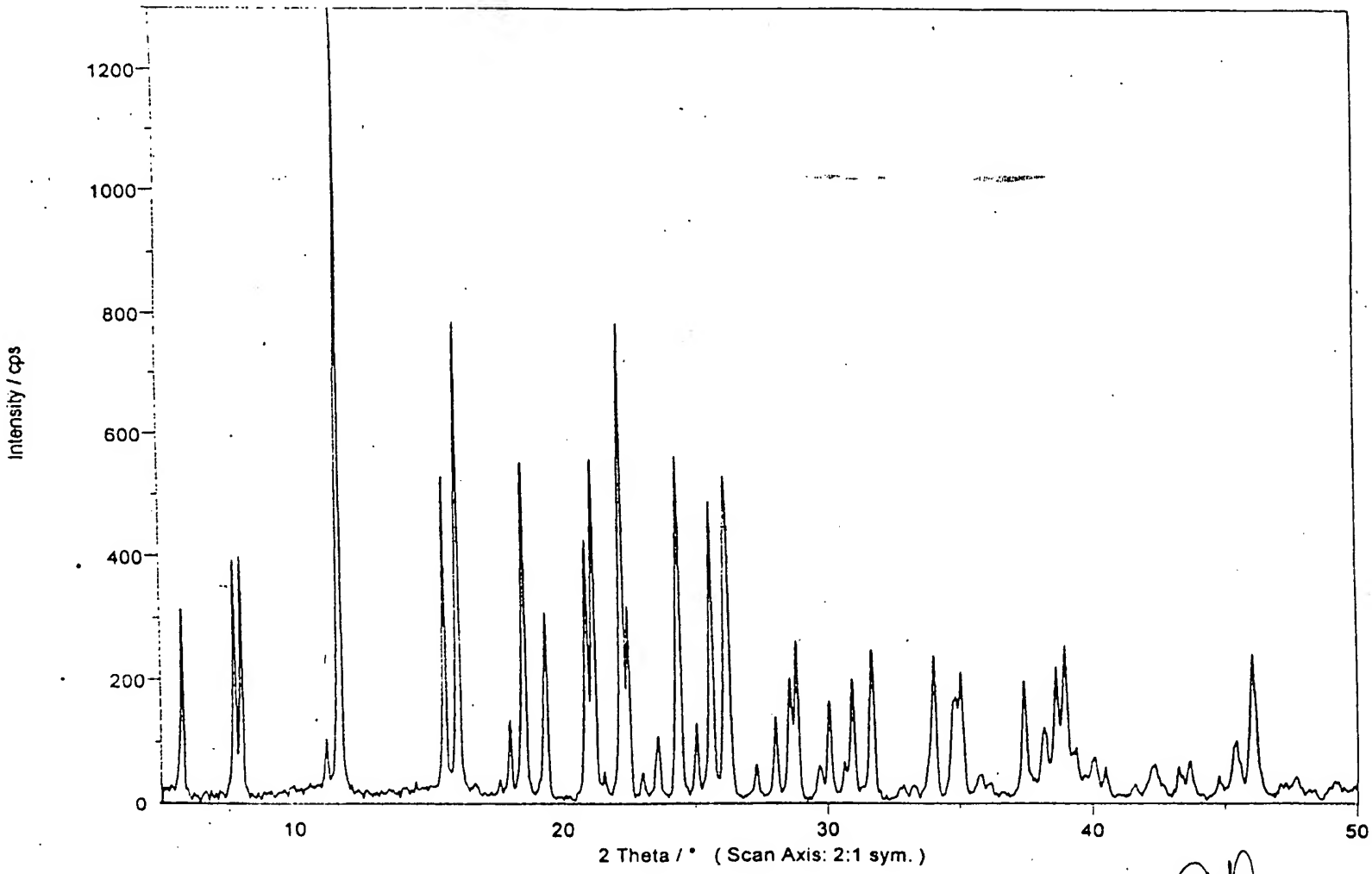
ABSTRACT

The present invention relates to the process for the preparation of novel crystalline form of Cefdinir, 7β-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid, herein called as Cefdinir Crystal B.

AUROBINDO PHARMA LIMITED
COMPLETE SPECIFICATIONS
APPLICATION NO. 440/MAS/2003

FIG. 1

TOTAL NO. OF SHEETS: 4
SHEET NO. 1



FOR AUROBINDO PHARMA LTD.

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DIRECTOR

AUROBINDO PHARMA LIMITED
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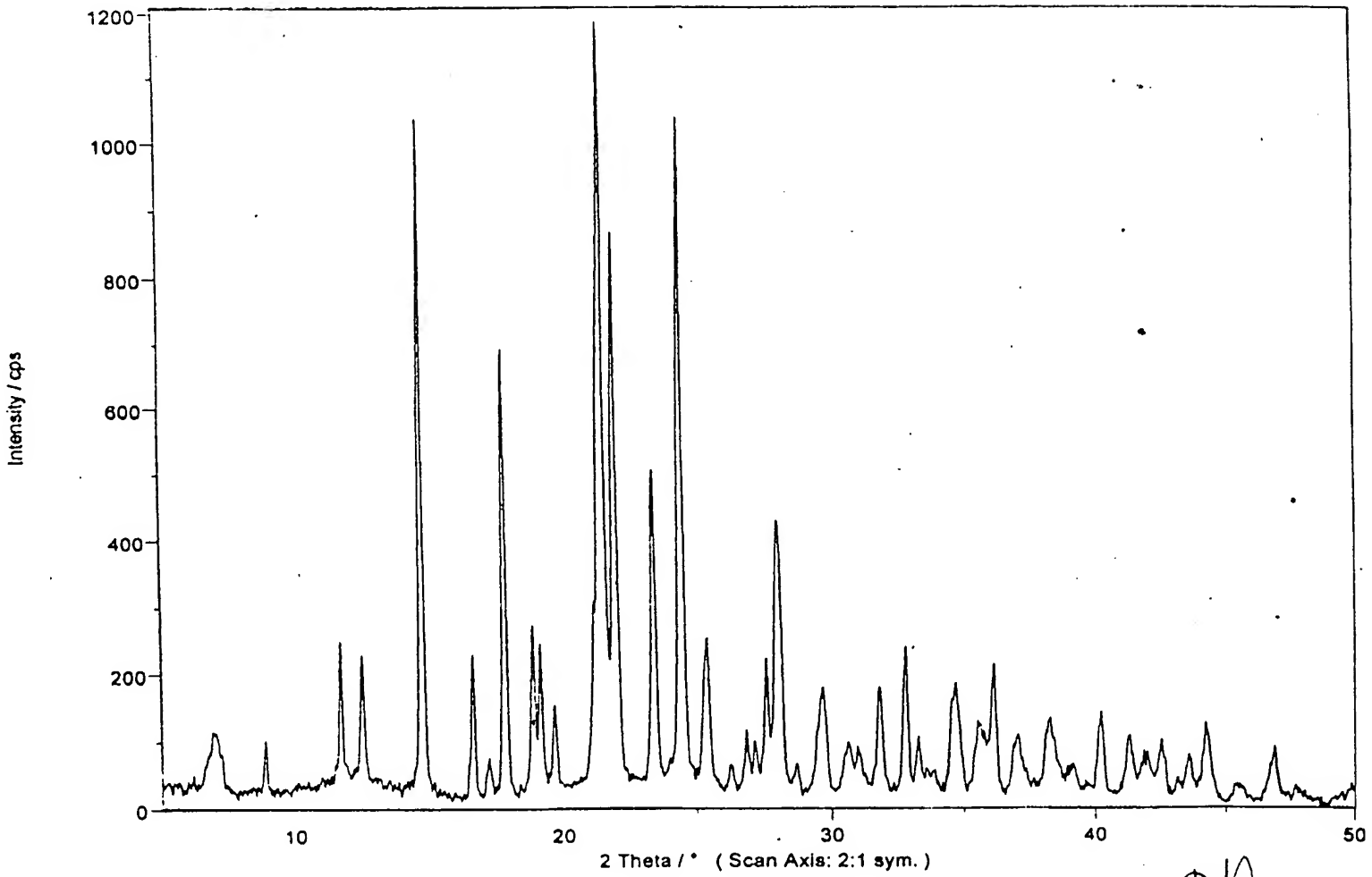
APPLICATION NO. 440/MAS/2003

FIG. 2

TOTAL NO. OF SHEETS: 4
SHEET NO. 2



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DIRECTOR

FIG. 3

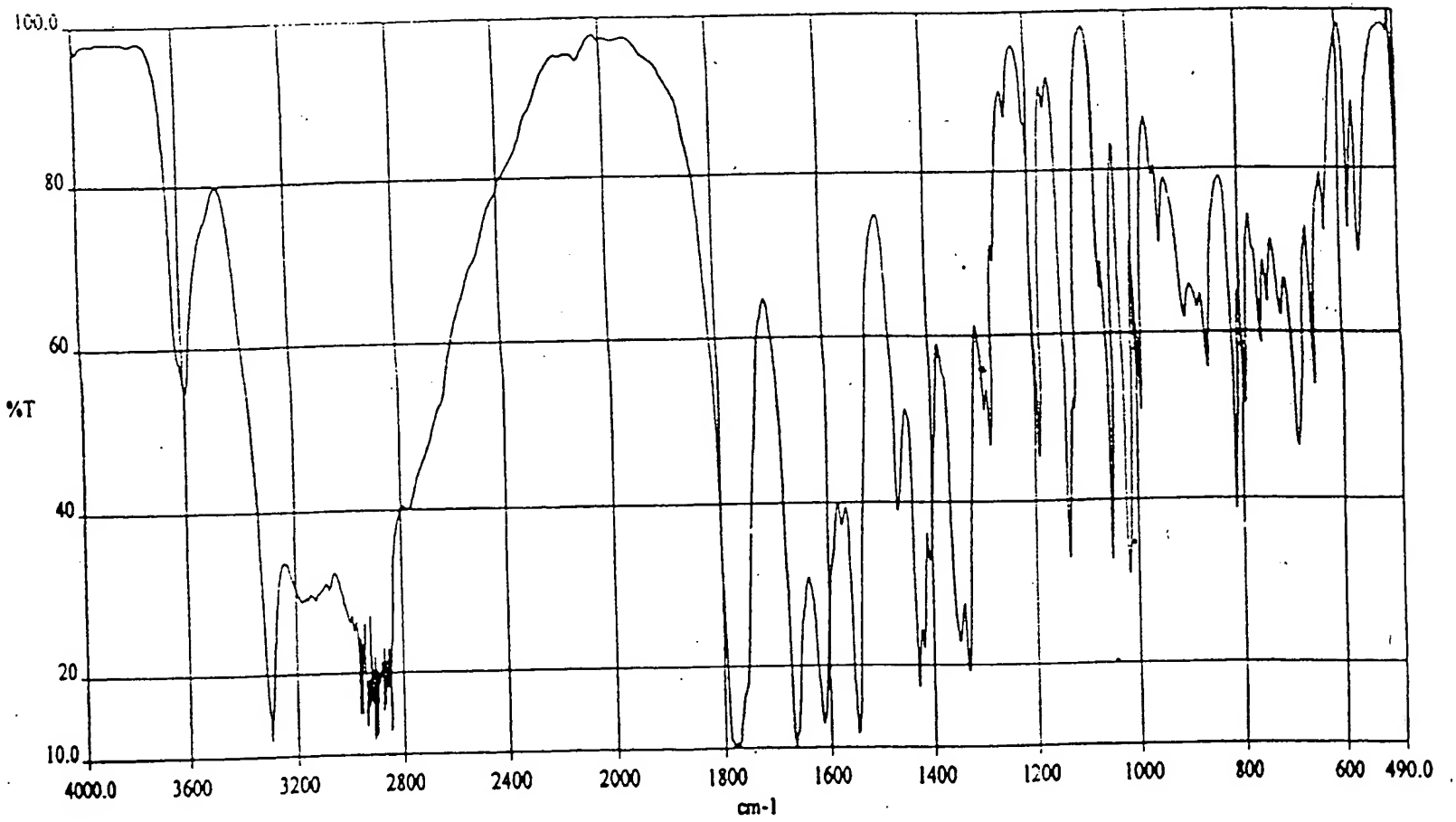

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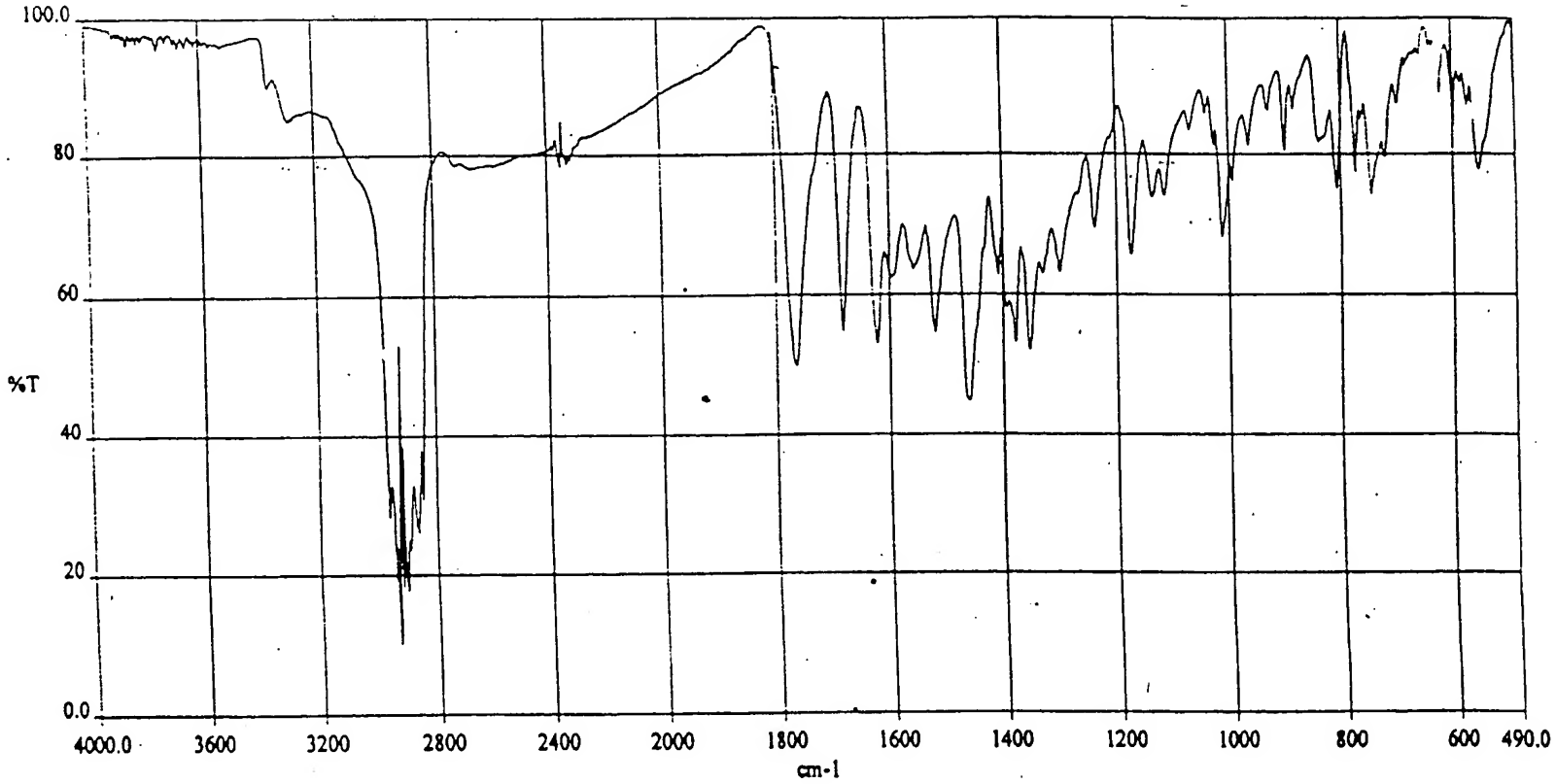
FIG. 4

TOTAL NO. OF SHEETS: 4
SHEET NO. 4



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DIRECTOR